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Ready, Set, Action: Potential Breakthrough Therapy for Treatment-Resistant Depression

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Abstract

Major depressive disorder is a psychiatric illness that is associated with a variety of debilitating symptoms such as persistent sadness, lack of interest and motivation, lassitude, pessimistic thoughts, and in severe cases, suicidal ideation and behavior. Current psychological and pharmacological treatments have been demonstrated efficacious; however, an ever-growing number of individuals frequently report minimal to no improvement with these treatments; and in some cases, a worsening of symptoms. This inadequacy to treatment is commonly known as treatment-resistant depression. At Kadima Neuropsychiatry Institute, Dr. Feifel treats individuals with treatment-resistant depression with advanced treatments such as TMS and ketamine. During my fieldwork internship at Kadima Neuropsychiatry Institute, my project focused on evaluating the efficacy of ketamine administered intramuscular to patients with treatment-resistant depression and determining which characteristics of a patient's psychedelic experience or "trip" is associated with the decrease in their depressive symptoms. The results of this project demonstrated that an initial low dose of ketamine was significantly quick and efficacious in decreasing depressive symptoms in patients with treatment resistant depressive. In addition, a first of its kind exploratory analysis suggested that the intensity, positive content, and dissociative characteristics of a ketamine induced psychedelic trip were strongly associated with the decrease in depressive symptoms. Despite the significance in these results, more research needs to include a larger sample and explore the specific subjective characteristics within a psychedelic "trip" to further understand its association with a decrease in depressive symptoms. The quick and efficacious antidepressant effects of ketamine demonstrated in this project provide much potential for a program involving a mobile ketamine clinic to address severe depression

and suicidality. Such therapeutic and intervention potentials can be explored further given an expansion of current policy limiting ketamine as a schedule III substance.

Introduction

Major depressive disorder is a burdensome psychiatric disorder that affects an individual's emotional, physical, and social abilities. Symptoms of major depressive disorder often include feelings of emptiness, diminished interest or pleasure in activities, decrease or increase in appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue, feelings of worthlessness, concentration difficulties, and, in severe cases, suicidal ideation and behavior, (American Psychiatric Association, 2013). According to the World Health Organization, depression is ranked as the leading cause of disability worldwide (Murry et. al., 1996). In addition, depression has been shown to be associated with a 15.9% risk of lifetime suicide attempt (Chen & Dilsaver, 1996). Despite the available psychological, pharmacological, and non-pharmacological treatment options for depression, a vast majority of individuals who have tried one or more of these options often report minimal to no improvement of their depressive symptoms. Researchers have defined this as treatment-resistant depression (Fava, 2003). Treatment-resistant depression is an ever-emerging category of major depressive disorder that physicians and researchers are determined to tackle.

Epidemiology of Major Depressive Disorder

A major depressive episode and a subsequent diagnosis of major depressive disorder can happen to anyone regardless of their age, gender, ethnicity, or socioeconomic status. The American Psychological Association (2013) defines a major depressive episode as a “persistent depressed mood and the inability to anticipate happiness or pleasure,” in a 2-week period that is represents a change from an individual's previous functioning. Between 2005 and 2014, 15.7 million people experienced a major depressive episode within the past years, in which 4.3% of adults 18 years and older had severe functional impairment, (Hedden et al., 2014). Furthermore,

the percentage of having a major depressive episode within the past year is highest for young adults aged 18-25 (9.3%), trailed by adults ages 26 to 49 (7.2%), then by those 50 years and older (5.2%). Although more prevalent in adolescents and adults, the prevalence rate of depression for children between ages of 3 to 17 is 2.1%, (Perou et al., 2013). The typical age-of-onset for major depressive disorder commonly begins in the early to mid-twenties. Individuals who experienced a major depressive episode during their adolescence and young adulthood are more likely to experience recurrent and severe major depressive episodes, causing severe psychosocial difficulties throughout adulthood, (Wilson et al., 2015). Women have been found to have a higher rate of a major depressive episode (9.5%) compared to men (5.6%) in all age groups, (Pratt & Brody 2014). Another main demographic that contributes to the rate of major depressive disorder is ethnicity. Severe depression rates have been found to be lower among Non-Hispanic white persons (2.6%) than Hispanic (3.7%) and Non-Hispanic black persons (4.1%); however, Non-Hispanic whites (37.0%) were found to seek a mental health care professional for severe depressive symptoms more than Hispanic (27.8%) and Non-Hispanic black (33.6%) persons (Pratt & Brody, 2014). Lastly, socioeconomic status contributes a major role in the onset of major depressive disorder. Individuals living below the poverty line are twice as likely to experience depressive symptoms than individuals living at or above the poverty level, (Pratt & Brody, 2014).

Given the range of individuals that suffer from moderate to severe major depressive disorder, a number of standard psychological, pharmacological, and non-pharmacological treatment options are available to attempt to alleviate the depressions debilitating symptoms. Despite the available treatment options for major depressive disorder, these treatment options are often reported to be non-efficacious or harmful.

Major Depressive Disorder Treatment

Cognitive behavioral therapy is a psychological treatment for depression that teaches patients strategic coping methods to address daily stressors and unhealthy thought patterns. This form of psychotherapy aims to modify and correct maladaptive psychological processes in order to boost an individual's happiness and positive cognition. Cuijpers et al. (2013) conducted a meta-analysis of cognitive behavioral therapy, and determined that the efficacy of psychotherapy is well supported; yet the long-term effects have been reported to be unfavorable, small, or even absent, (Conradi et al., 2017).

In general, individuals would rather seek pharmacological antidepressant medication rather than psychotherapy, yet antidepressant medication oftentimes demonstrate non-efficacy and intolerability. Jain et al. (2011) explained that achieving full remission takes adequate duration and dosage of antidepressants yet, individuals are reluctant to continue a prescribed regimen due to adverse side effects. Common complaints of antidepressant treatment, specifically SSRIs, are dry mouth, nausea, sleep disturbances, weight gain, sexual dysfunction, and suicidal ideation, (Ferguson, 2001; Zisook et al., 2009). In addition, 43% of individuals often report an inadequate response to the first line of antidepressant treatment; and 65-67% of individuals given a subsequent antidepressant trial had worse treatment compliance, due to perceived lack of treatment response and disease severity (Sicras-Mainar, et al., 2012).

Other than psychological and pharmacological treatment options, individuals will then turn to non-pharmacological treatments such as transcranial magnetic stimulation. Transcranial magnetic stimulation uses magnetic stimulations to activate deep brain regions and their interconnecting fibers to affect the mechanisms involved in the pathophysiology of depression, including the rewarding, motivation, and pleasure circuits. A full treatment cycle of transcranial

magnetic stimulation consists of a strict treatment schedule of thirty-six, twenty-minute daily treatment session at an outpatient psychiatry clinic. Levkovitz et al. (2015) demonstrated the efficacy of repetitive transcranial magnetic stimulation in treating individuals with major depressive disorder; yet also found that transcranial magnetic stimulation causes adverse side effects such as headaches and insomnia. Health Quality Ontario (2016) reviewed twenty-three randomized controlled trials of transcranial magnetic stimulation for treatment of treatment-resistant depression and concluded that there is a small, short-term effect compared to sham (placebo) treatment. Furthermore, results from the meta-analysis favored electroconvulsive therapy over transcranial magnetic stimulation for treating major depressive disorder.

In most severe cases of depression, individuals will often seek electroconvulsive therapy (ECT) as a last resort to gain remission. ECT is a procedure done under general anesthesia, in which small electrical currents are delivered to the brain, causing short seizures and, in turn, reversing symptoms of depression. A review of the efficacy of ECT demonstrated that the remission rate of ECT is short and often plagued with considerable cognitive side effects, which has been found to be worse among older populations (Charlson et al., 2012; Kumar et al., 2013).

Treatment-Resistant Depression and Ketamine

Treatment resistance to standard treatment options for depression are evident and disabling, validating treatment-resistant depression as a public health concern. Treatment-resistant depression is an emerging category of depression among individuals who have tried and failed prior treatments. Fava (2003) suggests that treatment-resistant depression is an inadequate response to at least one antidepressant trial of adequate doses and duration. Little (2003) defines treatment-resistant depression as being resistant (failure to produce significant clinical improvement) to at least two trials with antidepressants (adequate in dose, duration, and

compliance). Although definitions of treatment-resistant depression vary, the general and widely accepted criteria of treatment-resistant depression include: a clear diagnosis of major depressive disorder and treatment inadequacy and response to previous treatment trials, (Souery, et al., 1999).

In recent times, psychiatrist have been treating patients who have treatment-resistant depression with subanesthetic doses of ketamine, a common anesthetic that has been used since 1970. Subanesthetic doses of ketamine regularly produces dissociative, psychedelic, and most importantly, strong antidepressant effects. Subanesthetic doses of ketamine received intravenously have been demonstrated to produce quick and efficacious antidepressant effects when treatment individuals with treatment-resistant depression, (Feifel et al., 2017). Moreover, Xu et al., (2015) conducted a systematic review of 9 trials of ketamine treatment and concluded that low-doses of ketamine produce quick antidepressant effects; and showed a significant effect in reducing in suicidality within 1 to 3 days after treatment.

At present, treatment-resistant depression is a well-recognized category of depression that seems to be ever-growing. In light of inefficacious and intolerable standard treatments, physicians and researchers are at the forefront of exploring new breakthrough treatment options. Dr. David Feifel, the owner of Kadima Neuropsychiatry Institute, is one of those researchers at the forefront leading the way forward for breakthrough treatments like ketamine.

Scope of Work

Kadima Neuropsychiatry Institute is a specialty outpatient psychiatry clinic led by Dr. David Feifel who is an expert clinician and certified neuropsychiatrist. The mission at Kadima Neuropsychiatry Institute is to provide advanced therapeutic treatments such as repetitive transcranial magnetic stimulation (rTMS) and ketamine to individuals suffering from psychiatric

disorders, specifically treatment-resistant depression and posttraumatic stress disorder (PTSD). In addition, patients have the option of participating in sponsored clinical trials that investigates new psychiatric treatments. Overall, the vision of Kadima Neuropsychiatry Institute is to treat patients who are treatment-resistant to standard treatments for depression, while providing clinical evidence of the effectiveness and safety of new, breakthrough treatments for psychiatric disorders. To achieve the aforementioned, Dr. Feifel employs a team of six qualified health professionals: a chief finance officer, two registered nurses, two clinical research coordinators, and a medical biller/research assistant.

Given the robust clinical evidence of the quick antidepressant effects of ketamine (Drewniany et al., 2015; Feifel et al., 2017; Kishimoto et al., 2016), Dr. Feifel set up my fieldwork internship at Kadima Neuropsychiatry Institute to add to the literature of the efficacy of ketamine, and investigate what characteristics of a ketamine-induced psychedelic experience are important to a patient's decrease in depressive symptoms. See Appendix A for goals and objectives. My project focused on evaluating the efficacy of an initial dose of 0.25 mg/kg of ketamine administered intramuscular (IM) to real world patients with treatment-resistant depression and determining which characteristic of a patient's psychedelic experience or "trip" is associated with the decrease in their depressive symptoms. This project added to unanalyzed data that was collected at Dr. Feifel's outpatient clinic at the University of California, San Diego (UCSD). The dataset included 15 patients who received 0.25 mg/kg of ketamine intramuscular and completing the Patient History Questionnaire (PHQ-9) before and 24-hours after receiving ketamine treatment, and the Psychedelic Experience Survey (PES) after their psychedelic experience. The PHQ-9 is a commonly used 9-item self-report depression survey given to patients to gather a snapshot of their depressive symptoms over a specific time period, (Arroll et

al., 2010); see Appendix B for details. The PES is a Likert-type survey given to patients after their ketamine treatment to gather the subjective quality of the psychedelic experience, specifically the intensity, positive content, negative content, dissociation, hallucination, and adverse side effects (nausea/vomiting). Patients are asked to rate the quality of the aforementioned characteristics of their psychedelic experience on 5-point Likert-type scale, by which higher rating indicates a stronger quality; see Appendix C for details.

At Kadima Neuropsychiatry Institute, I reviewed patient charts to identify patients who had a primary diagnosis of treatment-resistant depression (inadequate response to their previous treatment trial) and received an initial intramuscular infusion of 0.25 mg/kg of ketamine. Of the 146 patient charts reviewed, 34 patients were recognized as having treatment-resistant depression and had received an initial dose of 0.25 mg/kg of ketamine. The 34 patient charts were also reviewed to identify those who completed both pretreatment PHQ-9, PES, and 24-hour post treatment PHQ-9. A total of 8 patients at Kadima Neuropsychiatry Institute met these criteria and were added to the dataset containing 15 patients from Dr. Feifel's UCSD outpatient clinic. It is important to note that the patient's included in this project were self-referred or referred by their treating physicians and psychiatrists and were not recruited for the purpose of the study. Once the patients were identified, their demographics (i.e., date of birth and sex), pretreatment PHQ-9 scores, PES scores, and 24-hour post treatment PHQ-9 scores were entered into the dataset using Microsoft Excel. The combined dataset was imported into a statistical package, R Commander, to run the appropriate analyses.

A total of 23 patients were analyzed in this study. To determine the efficacy of ketamine treatment, I ran a Paired t-test between pretreatment PHQ-9 scores and 24-hour post treatment PHQ-9 scores. To determine which characteristic of a patient's psychedelic experience or "trip"

was associated with the decrease in depressive symptoms, I ran a Pearson's R correlation between the separate items on the PES (intensity, positive content, negative content, dissociation, hallucination, and nausea and vomiting) and the percent difference (post treatment score minus pretreatment score divided by the post treatment score) of a patient's pretreatment PHQ-9 scores and 24 hour post treatment PHQ-9 scores. The dataset and initial analyses were provided to Dr. Feifel for further analysis and interpretation.

The individuals involved in this project were the preceptor (Dr. David Feifel) and myself, the research associate. This project was set to take real world clinical data and provide it to the literature of the efficacy of ketamine, and determine the importance of characteristics within a psychedelic experience and a decrease in depressive symptoms. My personal goal during this project was to accurately identify patients who were appropriate for the analyses and provide sound research and data for my preceptor to further analyze and interpret.

Health Impact

Results

The results of my fieldwork project at Kadima Neuropsychiatry Institute demonstrated the quick and efficacious effects of ketamine in decreasing depressive symptoms in real world patients with treatment-resistant depression. Additional analyses also demonstrated which characteristics of a patient's ketamine-induced psychedelic experience are most likely associated with their decrease in depressive symptoms. The dataset analyzed in this retrospective study included patients from Dr. Feifel's psychiatric outpatient clinic at UCSD (n=15) and Kadima Neuropsychiatry Institute (n=8).

All analyses were ran through the statistical package R Commander. According to the samples pretreatment PHQ-9 scores, the patients as a whole were moderately depressed, (M =

17.83, *SD* = 5.47). To determine the efficacy of ketamine treatment, pretreatment PHQ-9 scores and 24-hour post treatment PHQ-9 scores were analyzed using a Paired T-test. There was a significant decrease in PHQ-9 scores after receiving an initial intramuscular dose of 0.25 mg/kg of ketamine, t (22) = 5.27, $p < .001$. The average PHQ-9 score dropped to 13. 43 (*SD* = 6.69) 24 hours after receiving treatment, demonstrating quick antidepressant effects.

Descriptive statistics of the samples PES score are in Appendix D. To determine which characteristic of ketamine-induced psychedelic experience was most associated with a patient's depressive symptoms, Pearson correlations were ran between each item on the PES and the percent difference between pretreatment and 24-hour post treatment PHQ-9. There was a strong negative association between the intensity of a patient's psychedelic experience and their percent difference in pretreatment and 24-hour post treatment PHQ-9 scores, $r(21) = -0.69$, $p < .001$. There was a strong negative association between a patient's subjective positive experience and their percent difference in pretreatment and 24-hour post treatment PHQ-9 scores, $r(21) = -0.59$, $p < .001$. There was no association between a patient's subjective negative psychedelic experience and their percent difference in pretreatment and 24-hour post treatment PHQ-9 scores, $r(21) = -0.14$, $p = .51$. There was a significant negative moderate association between a patient's dissociative experience during their psychedelic experience and their percent difference in pretreatment and 24-hour post treatment PHQ-9 scores, $r(21) = -0.46$, $p < .02$. There was no association between hallucinations during a patient's psychedelic experience and their percent difference in pretreatment and 24-hour post treatment PHQ-9 scores, $r(21) = -0.31$, $p = .15$. Lastly, there was no association between adverse effects (nausea and vomiting) during a patient's psychedelic experience and their percent difference in pretreatment and 24-hour treatment PHQ-9 scores, $r(21) = -0.24$, $p = .27$.

The results of this retrospective study demonstrated the efficacious antidepressant effects of an initial intramuscular dose of 0.25 mg/kg of ketamine for the treatment of treatment-resistant depression. Our results were consistent with the literature in that ketamine is a quick and efficacious option for individuals with treatment-resistant depression, (Drewniany et al., 2015; Feifel et al., 2017; Kishimoto et al., 2016). In addition, our exploratory analyses suggested that there is an important association of the intensity, positive content, and dissociative characteristics of a psychedelic experience and the decrease in depressive symptoms. To our knowledge, these exploratory findings are the first of its kind in regard to ketamine treatment for treatment-resistant depression. Although these consistent and new findings are key to addressing the need for more quick and efficacious treatments for depression, more research needs to be done to expand on and validate which characteristics of ketamine's psychedelic "trip" are crucial to its antidepressant effects.

Implications

Given the inadequacy of standard treatment options for depression and the ever-growing prevalence of treatment-resistant depression, more research needs to delve into ketamine's strong and quick antidepressant effects, as demonstrated in my fieldwork project, to unleash its true antidepressant potential. Although the results from this fieldwork project were informative, the sample was relatively small and only included San Diego based patients who can afford ketamine treatment, which was $400 for the initial dose of 0.25 mg/kg and a commitment to at least five subsequent treatments at the same price. Further ketamine research needs to increase sample selection and size to confirm the results account for all the variability in the general population, thus ensuring the results are generalizable. In addition, our exploratory analyses demonstrated broad characteristics of a psychedelic experience. The PES used in the study is

limited to broad categories without delving into specifics qualities of each characteristic. Future research needs to address this limitation and expand on what specific subjective experience is important to ketamine's antidepressant effects. Expanding on the specifics of the positive content of a psychedelic ketamine experience could be especially crucial to addresses opposing negative content associated with depression such as pessimistic thoughts and suicidal ideation and behavior.

Given the exploratory results of my fieldwork project, future programs addressing severe depression and suicidality need to capitalize on the quick antidepressant and positive content emitting effects of ketamine treatment. To my knowledge, creating a mobile on demand ketamine clinic within our country would be the first of its kind. A start up pilot trial could be created to determine whether the ketamine treatment for severe depression associated with suicidality could overall decrease the risk of suicide within the United States. The prospective success of such a program could give positive insight into ketamine’s impact on mental health in the United States. Such success and impact could possibly lead to re-examining the policies restricting ketamine’s powerful potential.

Despite being an available, yet expensive, treatment option for treatment-resistant depression, the therapeutic effects of ketamine seem to be restrained by current policy and regulations. Currently ketamine is listed as a schedule III drug controlled substance and is only the US Food and Drug Administration (FDA) approved as a general anesthetic; however, psychiatrist and anesthesiologist often use it “off-label” for treating chronic pain and treatment-resistant depression. The Controlled Substances Act is a statute that establishes drug policies that regulate the professional and recreational use of drugs. Even though ketamine is not a strictly regulated schedule I or II substance, its street reputation and recreational history for abuse inhibit

researchers from important future research. Although the broad regulation on drugs are undeniably needed, ketamine and its newfound therapeutic effects for depression need our efforts to explore different policies that allow more research and utilization of its potential therapeutic uses. Expanding policy to increase the accessibility of ketamine would be a step closer to unleashing ketamine therapeutic potential for depression as well as exploring its potential for more indications.

Conclusion

This fieldwork project at Kadima Neuropsychiatry Institute focused on evaluating an advanced specialty treatment that addresses an ever-growing subcategory of major depressive disorder known as treatment-resistant depression. Although there are a number of standard psychological, pharmacological, and non-pharmacological treatment options for major depressive disorder, the majority of patients taking these standard treatments often report minimal to no improvement of their depressive symptoms. This reported inadequacy to standard treatment has been commonly defined as treatment-resistant depression, (Fava, 2003; Little, 2009). To address this growing population, ketamine treatment has been demonstrated to be an efficacious antidepressant treatment for patients with treatment-resistant depression (Feifel et al., 2016). Within my fieldwork project at Kadima Neuropsychiatry Institute with Dr. David Feifel, I evaluated the efficacy of an initial intramuscular dose of 0.25 mg/kg of ketamine administered intramuscular in real world patients with treatment-resistant depression, and explored which characteristic of their ketamine induced psychedelic experience or “trip” was most associated with the decrease in depressive symptoms. See Appendix E for Competency Matrix.

After reviewing patient charts for individuals who consented to receiving ketamine treatment and partaking in the necessary self-report surveys, a total of 24 patients’ pretreatment

PHQ-9, PES, and 24-hour post treatment PHQ-9 scores were imported into a statistical package, R Commander, to analyze. The results of the analyses confirmed ketamine's quick antidepressant effects and suggested that having an intense, positive, and dissociative psychedelic experience or "trip" are important characteristics in ketamine's antidepressant effects. Within the sample of this project, there was a significant decrease in a patient's overall depressive symptoms within 24 hours after receiving an initial dose of ketamine. Also, those that reported having an intense, positive, and dissociative experience during their ketamine induced psychedelic experience were more likely to indicate a decrease in their depressive symptoms.

Although the demonstrated efficacy of ketamine in this project were consistent with the literature, more research needs to be done to strengthen the findings of this project by increasing the sample size and selection to give such results more inference and power. Furthermore, given the newfound importance of intensity, positive content, and dissociation within a ketamine induced psychedelic experience, a public health program, such as a mobile ketamine clinic, needs to be developed to capitalize on ketamine's elicitation of an intense and positive experience in order to address the need of those who often ruminate on the negativity and suicidality. Given the findings of this project and the potential of ketamine as a therapeutic medication rather than just an analgesic, individuals suffering from treatment-resistant depression could experience such efficacious potential once current legislation and policies are expanded to allow ketamine to be further researched for its quick and therapeutic properties.

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Appendices

Appendix A

Goals and Objective

Goal: Conduct a retrospective study to determine the efficacy of ketamine administered intramuscular to real world, clinical patients with treatment-resistant depression; and determine which characteristics of a psychedelic experience is associated with the decrease in depression symptoms.				
Objective(s)	**Activities**	**Start/End Date**	**Who is Responsible**	**Tracking Measures**
Identify and select patients who completed ketamine treatment at Kadima Neuropsychiatry Institute	- Review patient charts and database - enter in demographics (e.g., age and sex) in excel	11-Sep-2017 to 08-Oct-2017	- Research associate - Investigator	Investigator will review identified patients.
Review patient rating scales such as the Patient Health Questionnaire (PHQ) and the Psychedelic Experience Questionnaire (PES).	- organize each patient's rating scales with respect to time of treatment (e.g., before ketamine treatment, 24 hours after ketamine treatment).	09-Oct-2017 to 29-Oct-2017	- Research associate - Investigator	Investigator will review rating scale and treatment schedule
Prepare spreadsheet with patient demographics and rating scales for analysis.	- Enter in appropriate data into excel and R.	30-Oct-2017 to 26-Nov-2017	- Research associate - Investigator	Investigator will review spreadsheet before analysis.
Analyze treatment rating scales (i.e., PES and PHQ) scores of the identified patients	- R analysis	27-Nov-2017 to 04-Dev-2017	- Research associate - Investigator	Investigator will review SPSS analysis

Appendix B

Name:
Date:

Patient Health Questionnaire – 9 (PHQ-9)
Ketamine Follow up

Over the past 24hrs, how often have you been bothered by any of the following problems?	Not at all	Some of the time	More than half the time	Nearly all the time
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or letting your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or hurting yourself in some way	0	1	2	3
			Total:	

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
☐	☐	☐	☐

Appendix C

Psychedelic Experience Survey

Name:	Date:	Time:
Age:	Medication: *Ketamine*	
Gender:	Total Dose:	

For each item below, circle the number to the right that best fits your judgement of its quality. Use the rating scale to select the quality number.

Characteristics of experience in clinic	Scale				
	None to Mild	Moderate			Substantial
1. Overall intensity of "trip"	1	2	3	4	5
2. **Positive** emotional content	1	2	3	4	5
3. **Negative** emotional content	1	2	3	4	5
4. Dissociative / "out of body" sensation	1	2	3	4	5
5. Hallucinations	1	2	3	4	5
6. Nausea / vomiting	1	2	3	4	5
7. New insight	1	2	3	4	5

8. Please describe the experience: (as the use of psychedelic treatment is a novel approach to the treatment of refractory depression, our patients are an invaluable source of information; please feel free to share anything you remember about your response to this medication while it is still fresh in your mind.)

Version 1 (01Sep2017)

Appendix D

Table 1
Mean and Standard Deviation of PES Items

Items	M	SD	n
Intensity	2.80	1.35	23
Positive Content	2.85	1.26	23
Negative Content	1.30	0.56	23
Dissociation	2.28	1.29	23
Hallucination	1.43	0.79	23
Nausea/Vomiting	1.17	0.65	23

Appendix E

Competency Matrix

Competency	Method of Achievement
1. Applied epidemiological methods to the breadth of settings and situations in public health practice	I discussed and worked with preceptor to determine the appropriate epidemiological research method carried out for my fieldwork project according to the public health concern (treatment-resistant depression), intervention (ketamine), and population type (cash pay patients).
2. Selected quantitative and qualitative data collection methods appropriate for a given public health context	Developed the Psychedelic Experience Survey (PES) to gather critical information of a patient's psychedelic trip. Selected the Patient Health Questionnaire (PHQ) to determine if there is a linear correlation between patient's PES and PHQ scores.
3. Analyzed quantitative and qualitative data using biostatistics, informatics, computer-based programming and software, as appropriate	I ultimately analyzed patients PES and PHQ scores using Excel and R.
4. Interpreted results of data analysis for public health research, policy or practice Public Health & Health Care Systems	Interpreted results of patient PES and PHQ scores. Once interpreted, these findings will be further analyzed by preceptor and will thus be used in clinical practice.
19. Communicated audience-appropriate public health content, both in writing and through oral presentation	After findings are analyzed, I will create a newsletter that will display recent finding, their significance, and the potential successes with ketamine treatment. This newsletter will be provided to local health care providers as well at professionals in network with the organization.